

REMARKS

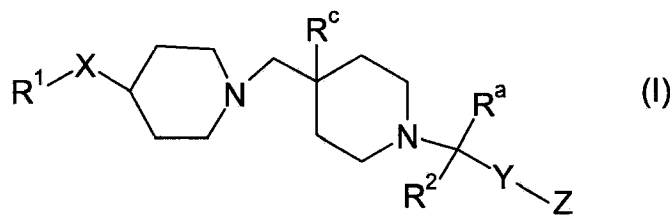
In response to the final office action dated August 26, 2008, Applicants have amended claim 1 and cancelled claims 7, 13, and 14. Claims 3 and 10-12 were cancelled or withdrawn in prior amendments. Claims 1, 2, 4-6, 8, and 9 are presented for examination.

Initially, Applicants appreciate with thanks the Examiner's indication that the obviousness rejection of claim 6 has been withdrawn. Further, Applicants note that the Examiner examined previously withdrawn claim 8 in this office action. Applicants assume that the Examiner has rejoined claim 8 and therefore has listed this claim as a pending claim.

Rejection under 35 U.S.C. §103(a)

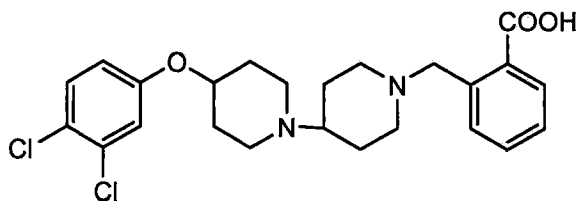
Claims 1, 2, 4, 5, and 7-9 are rejected as being obvious over Lawrence et al. WO 2001/077101 ("Lawrence") in view of Ko et al., WO 2000/35877 ("Ko").

Among pending claims 1, 2, 4, 5, 8, and 9, independent claim 1 is discussed first. Claim 1, as amended, covers compounds of formula (I):



in which X is O; Y is a bond or C₁₋₆ alkylene optionally substituted by C₁₋₄ alkyl or phenyl; Z is CO₂R^b, NHS(O)₂CF₃, S(O)₂OH, OCH₂CO₂R^b or tetrazolyl; R¹ is aryl; R² is hydrogen, C₁₋₆ alkyl, aryl or heterocyclyl; R^a and R^b are, independently, hydrogen or C₁₋₄ alkyl; or when R² is aryl or heterocyclyl R^a optionally is C₂₋₃ alkylene forming a ring with an ortho position on R²; and R^c is hydrogen or hydroxyl. In the compounds of amended claim 1, Y can no longer be a phenylene group. Thus, Z (e.g., CO₂R^b) cannot be attached to a piperidine ring through a phenylene group. Instead, Z can only be attached to a piperidine ring through an alkylene group.

Lawrence describes using bipiperidine compounds for treating a chemokine or H1 mediated disease. *See*, e.g., the abstract. However, Lawrence does not disclose or suggest the compounds of amended claim 1. The Examiner points to the following compound described in



Lawrence: , and states that “the rejection is still valid because the compound that was the basis of the rejection is another species of the specification that is claimed.” *See* the final office action, page 3, lines 2-4. However, the Lawrence compound shown above is significantly different from the compounds of amended claim 1. Specifically, as discussed above, in the compounds of amended formula 1, Z (e.g., CO₂R^b) is attached to a piperidine ring through an alkylene group only, which does not include a phenylene group. By contrast, the group in the Lawrence compound that corresponds to Z, i.e., COOH, is attached to a piperidine ring through a phenylene group. Lawrence does not disclose or render obvious bipiperidine compounds in which Z (e.g., CO₂R^b) is attached to a piperidine ring only through an alkylene group, as required by amended claim 1. Thus, amended claim 1 is not obvious over Lawrence.

Ko does not cure the deficiencies in Lawrence. Ko describes bipiperidine compounds as modulators of chemokine receptors. *See*, e.g., the abstract. It also describes numerous bipiperidine compounds containing a functional group Z directly attached to one of the two piperidine rings, Z being C(O)R³, S(O)₂R³, C(O)OR³, C(O)NR²R³, C(=NR¹)NR²R³, C(=CHCN)NR²R³, C(=CHNO₂)NR²R³, C(=C(CN)₂)NR²R³, or (CR¹R²)t-phenyl substituted with 0-5 R¹⁵. *See*, e.g., claim 1 of Ko. Similar to Lawrence, Ko does not disclose or render obvious compounds of formula (I) in which Z is attached to a piperidine ring through an alkylene group, as required by amended claim 1. Thus, even if Ko and Lawrence were combined, the results would not have been the compounds of amended claim 1.

For at least the reasons set forth above, amended claim 1 is not obvious over Lawrence in view of Ko. Since claims 2, 4, 5, 8, and 9 depend from amended claim 1, they are also not obvious Lawrence in view of Ko. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Double patenting rejections

The Examiner rejects claims 1, 2, and 4-9 under the judicially created doctrine of obviousness-type double patenting on three grounds, each of which is traversed below.

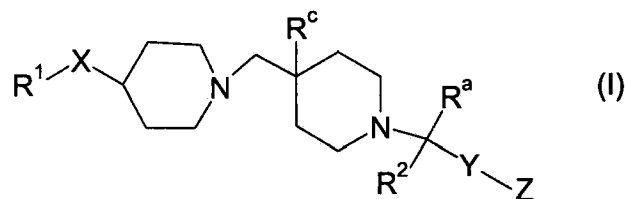
I

Claims 1, 2, and 4-9 are provisionally rejected as being obvious over claims 1, 2, 4-7, and 9-11 of copending Application No. 10/508,331 ("the '331 application"). Applicants request that this rejection be held in abeyance and will consider filing a terminal disclaimer with respect to the '331 application when the pending claims are otherwise deemed in condition for allowance.

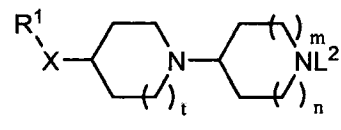
II

Claims 1, 2, and 4-9 are rejected as being obvious over claims 1-4 and 9-18 of U.S. Patent No. 7,179,922 ("the '922 patent").

Among pending claims 1, 2, 4-6, 8, and 9, independent claim 1 is discussed first. Claim 1, as amended, covers compounds of formula (I):



, which contain a methylene group between two piperidine rings. In formula (I), Y is a bond or C₁₋₆ alkylene optionally substituted by C₁₋₄ alkyl or phenyl and Z is CO₂R^b, NHS(O)₂CF₃, S(O)₂OH, OCH₂CO₂R^b or tetrazolyl. By contrast, claims 1-4 and 9-18 of the '922 patent cover compounds of the following formula:



compounds of claims 1-4 and 9-18 of the '922 patent are significantly different from those of claim 1 of the present application. First, the compounds of claims 1-4 and 9-18 of the '922 patent do not have a methylene group between the two piperidine rings, as required by the compounds of claim 1 of the present application. Second, L² in the compounds of claims 1-4 and 9-18 of the '922 patent is significantly different from its corresponding group, i.e., C(R^aR²)-Y-Z, in the compounds of claim 1 of the present application. For example, when L² is t-butoxycarbonyl, it differs from C(R^aR²)-Y-Z in that the latter group contains at least one

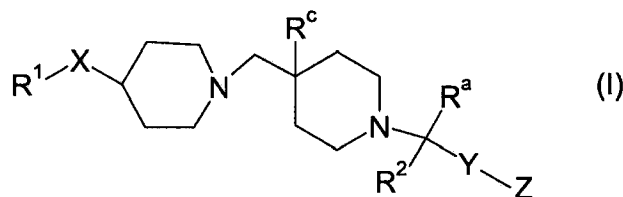
methylene group between Z and a piperidine ring. As another example, when L^2 is benzyl, it is significantly different from $C(R^aR^2)-Y-Z$ in that L^2 does not include any of the groups assigned to Z recited in claim 1 of the present application. Given the significant structural differences, it would not have been obvious for one skilled in the art to modify the compounds of claims 1-4 and 9-18 of the '922 patent to provide the compounds of claim 1 of the present application.

Thus, claim 1 is not obvious over claims 1-4 and 9-18 of the '922 patent. Since claims 2, 4-6, 8, and 9 depend from claim 1, they are also not obvious over claims 1-4 and 9-18 of the '922 patent. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

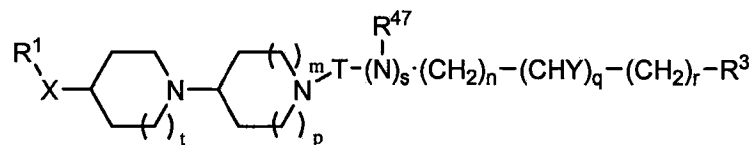
III

Claims 1, 2, and 4-9 are rejected as being obvious over claims 1-8 and 10-13 of U.S. Patent No. 6,903,115 ("the '115 patent").

Among pending claims 1, 2, 4-6, 8, and 9, independent claim 1 is discussed first. Claim 1, as amended, covers compounds of formula (I):



, which contain a methylene group between two piperidine rings. In formula (I), Y is a bond or C_{1-6} alkylene optionally substituted by C_{1-4} alkyl or phenyl and Z is CO_2R^b , $NHS(O)_2CF_3$, $S(O)_2OH$, $OCH_2CO_2R^b$ or tetrazolyl. By contrast, claims 1-8 and 10-13 of the '115 patent cover compounds of the following formula:



, in which R^3 is heterocycl. The compounds of claims 1-8 and 10-13 of the '115 patent are significantly different from those of claim 1 of the present application. First, the compounds of claims 1-8 and 10-13 of the '115 patent do not have a methylene group between the two piperidine rings, as required by the compounds of claim 1 of the present application. Second, R^3 (which corresponds to Z recited in formula (I)) in the compounds of claims 1-8 and 10-13 of the '115 patent is heterocycl. The '115 patent does not disclose or render obvious compounds of formula (I) in which Z (which

corresponds to R^3 in the formula recited in claim 1 of the '115 patent) is CO_2R^b , $NHS(O)_2CF_3$, $S(O)_2OH$, $OCH_2CO_2R^b$ or tetrazolyl, as required by amended claim 1 of the present application. Given these significant structural differences, it would not have been obvious for one skilled in the art to modify the compounds of claims 1-8 and 10-13 of the '115 patent to provide the compounds of claim 1 of the present application.

Thus, claim 1 is not obvious over claims 1-8 and 10-13 of the '115 patent. Since claims 2, 4-6, 8 and 9 depend from claim 1, they are also not obvious over claims 1-8 and 10-13 of the '115 patent. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Please apply any charges to deposit account 06-1050, referencing Attorney's Docket No. 06275-0448US1.

Respectfully submitted,

Date: October 27, 2008

/Tony Zhang/

Tony Zhang, Ph.D.
Reg. No. L0256

Fish & Richardson P.C.
Citigroup Center - 52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291
30453561.doc